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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,134	10/19/2005	Maurice Goldman	PS0268	6654

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IP DEPARTMENT
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EXAMINER	
SCHLIENTZ, LEAH H	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
08/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,134	GOLDMAN ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *12-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 1/23/08 is acknowledged.

Status of Claims

Claims 1 – 18 are pending, of which claims 12 – 18 are withdrawn from consideration at this time as being drawn to a non-elected invention. Claims 1 – 11 are readable upon the elected invention and are examined herein on the merits for patentability.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 – 11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a method for producing an MR contrast agent, the method comprising the steps of: -obtaining a

solution in a solvent of a hydrogenatable, unsaturated substrate compound and a catalyst for the hydrogenation of a substrate compound, wherein the substrate compound comprises imaging nuclei. However, the specification does not provide description of the claimed hydrogenatable, unsaturated substrate compound required to make and use the contrast agent as broadly claimed. There is no description provided regarding which types of specific chemical moieties are used to represent the substrate that would render such a compound to be useful as a contrast agent. There is very little predictability in the art concerning any undefined species which may represent a substrate compound and furthermore, one of ordinary skill in the art would not know which chemical moiety would represent a substrate out of an almost unlimited number of chemical species which may be possible. The specification does not provide any guidance to the specific identity or physical / chemical structure of the variables which represent a substrate, and because the structures and physical identities of these elements are undefined, it is unclear how Applicant envisaged suitable elements to satisfy the functional requirements of the substrate. It is noted that the specification refers to suitable substrate materials as those found in WO 99/24080, however, the incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the

material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 – 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to a method for producing MR contrast agent comprising the steps of -*obtaining* (100) a solution in a solvent of a hydrogenatable, unsaturated substrate compound...; -*hydrogenating* (110) the substrate...; and -*exposing* (120) the contrast agent to a oscillating magnetic field in combination with a stationary magnetic field. Dependent claims 7 – 10 further include various –*applying* (420), or (430-480), or (470), or (520), or (530-540), or (570), etc. and -*waiting* (540) or (580), etc. steps. The numbers included in parenthesis appear to refer to various figures in the specification (see Figures 1 – 5). However, where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." Ex parte Fressola, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations omitted). Reference characters

corresponding to elements recited in the detailed description and the drawings may be used in conjunction with the recitation of the same element or group of elements in the claims. See MPEP § 608.01(m). See also 2173.05(s). In the instant case, the claims appear to be adequately described using text and the reference to the figures via various step numbers is unnecessary. It is respectfully suggested that the claims should be amended to remove the step numbers in parentheses.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Ardenkjaer-Larson *et al.* (WO 99/35508, whereby US 6,278,893 is relied upon as equivalent).

Ardenkjaer-Larson discloses methods of magnetic resonance investigation of a sample comprising the step of ex vivo polarisation of a high T_1 agent wherein the polarising agent is optionally separated from the high T_1 agent before the high T_1 agent is administered to the sample (abstract). The methods of Ardenkjaer-Larson include the following steps: (i) subjecting a high T_1 agent to ex vivo polarisation; (ii) optionally exposing the high T_1 agent to a uniform magnetic field (e.g. the primary field B_0 of the imaging apparatus of a weaker field) and (v) exposing the sample to a second radiation

of a frequency selected to excite nuclear spin transitions in a selected nuclei (e.g. the MR imaging nuclei of the high T_1 agent) (see column 2, lines 5 – 30). With regard to step (i), ex vivo polarisation may be carried out by any known method, and by way of example are four such methods described by Ardenkjaer-Larson (column 12, lines 58+). One such method of ex vivo polarisation is effected by para-hydrogen enriched hydrogen gas. A high T_1 agent suitable for use in such a method is hydrogenatable and includes one or more unsaturated bonds (column 17, line 43 – column 18). The hydrogenation is performed in the presence of a catalyst (column 20, line 35). Hydrogenation takes place in aqueous or nonaqueous solution (column 22, lines 1 – 44). With regard to step (v), see Examples 3 and 4, whereby polarized samples are inserted into a spectrometer or MRI machine and ^{13}C spectra are recorded. One of ordinary skill would recognize that with regard to steps (iii) and (v) of Ardenkjaer-Larson, the act of taking ^{13}C spectra would inherently involve the steps of exposure of the sample to stationary (e.g. B_o) and oscillating magnetic fields (e.g. RF pulse), e.g. as in "a frequency selected to excite nuclear spin transitions," as taught by Ardenkjaer-Larson (column 2, lines 20 - 21). It is noted that Ardenkjaer-Larson teaches steps in addition to those claimed, e.g. administration to patient before exposure to radiation of a frequency to excite nuclear spin transitions, etc. However, the comprising language of the instant claims does not preclude the presence of additional steps, accordingly Ardenkjaer-Larson meets the claims.

Claims 1 – 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Golman *et al.* (WO 99/24080, whereby US 6,574,495 is relied upon as equivalent).

Golman discloses methods of magnetic resonance investigation of a sample which relies on ex vivo nuclear polarization of a selected non-hydrogen, non-zero imaging nuclei (e.g. ^{13}C), of an MR imaging agent by reaction of a precursor with para-hydrogen enriched hydrogen gas. The method comprises (i) reacting para-hydrogen enriched hydrogen with a hydrogenatable MR imgaging agent precursor containing a non-hydrogen non-zero nuclear spin nucleus to produce a hydrogenated MR imaging agent; (ii) administering said hydrogenated MR imaging agent to said sample; (iii) exposing said sample to radiation of a frequency selected to excite nuclear spin transitions of said non-zero nuclear spin nucleus in said hydrogenated MR imaging agent; (iv) detecting magnetic resonance signals of said non-zero nuclear spin nucleus from said sample (column 2, lines 25 – 55). The hydrogenation step preferably is performed in liquid or gaseous phase, in the presence of catalyst (column 3, lines 35 – 40). MR imaging precursors are hydrogenatable and preferably include one or more unsaturated bond (column 4, lines 21 – 24). It is desirable to carry out the hydrogenation step in a very low magnetic field (column 13, lines 1 - 15). One the MR imaging agent has been administered, chosen procedures for detecting MR signals are that which is well known from conventional MR scanning. Such conventional MR scanning includes a primary magnetic (i.e. stationary) and RF pulses (i.e. oscillating). When the MR signal derives from hyperpolarization of the reporter nuclei, the signal must be recovered following a train of 180° RF pulses (column 19, lines 5 – 20). With

regard to instant claim 3, Golman teaches that the Larmor frequency of carbon is about 10 MHz at 1 T, and thus the rf-absorption in a patient is less than in ^{1}H imaging (column 17, lines 45 – 50). With regard to claims 8 – 11, Golman teaches various pulse sequences which appear to meet the instant limitations (e.g. pulse 180, 90, waiting for t/2, etc.). See column 19 – 20. It is noted that Golman teaches steps in addition to those claimed, e.g. administration to patient before exposure to radiation of a frequency to excite nuclear spin transitions, etc. However, the comprising language of the instant claims does not preclude the presence of additional steps, accordingly Golman meets the claims.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS